1. Title, Protocol ID, IRB number

English: Special Care Patterns for Elderly HNSCC Patients Undergoing Radiotherapy (SENIOR)

German: Klinisches Ansprechen und Verträglichkeit von Radio(chemo)therapie bei älteren Patienten mit Kopf-Hals-Tumoren

Protocol ID: FRKS003723

IRB number of the Ethics Committee Freiburg: 551/18

2. Synopsis

PIs	**Prof. Dr. Dr. Nils H. Nicolay, M.D., Ph.D.** Department of Radiation Oncology, University Medical Center Freiburg Robert-Koch-Str.3, 79106 Freiburg, Germany Tel: +49 (0) 761 270-95200 Fax: +49 (0) 761 270-94720 Mail: nils.nicolay@uniklinik-freiburg.de and **Dr. Alexander Rühle, M.D.** Department of Radiation Oncology, University Medical Center Freiburg Robert-Koch-Str. 3, 79106 Freiburg, Germany Tel: +49 (0) 761 270-94520 Fax: +49 (0) 761 270-94720 Mail: alexander.ruehle@uniklinik-freiburg.de
Title	Special Care Patterns for Elderly HNSCC Patients Undergoing Radiotherapy (SENIOR)
Patient Population	Elderly patients (≥65 years) with head-and-neck squamous cell carcinomas undergoing definitive (chemo)radiotherapy
Aims	To determine the value of concomitant chemotherapy in elderly patients with locally advanced head-and-neck squamous cell carcinoma (HNSCC) undergoing definitive (chemo)radiotherapy. In particular, subgroup analyses based on age, performance status and comorbidity burden are planned in order to define the benefit of chemotherapy in distinct subgroups. Furthermore, patterns-of-care regarding the administration of concomitant chemotherapy will be analyzed within this international cohort.
Intervention	No intervention
Inclusion and Exclusion Criteria	**Inclusion Criteria:** • definitive (chemo-)radiotherapy of locoregionally advanced (cT3-4 and/or cN+) head-and-neck squamous cell carcinomas (HNSCC) of the oral cavity, oropharynx, hypopharynx or larynx • primary treatment between 2005 and 2019 • age ≥65 years at the time of (chemo-)radiotherapy **Exclusion Criteria:** • adjuvant (chemo-)radiotherapy • induction chemotherapy • history of previous head-and-neck cancers or radiotherapy in the head-and-neck region • distant metastases at (chemo-)radiotherapy initiation (cM1)

	• HNSCCs of the nasopharynx, salivary glands, skin or with unknown primary
Outcome Measure	Primary: • Overall survival (OS) Secondary: • Progression-free survival (PFS) • Type of concomitant chemotherapy • Cumulative cisplatin dose • Radiotherapy completion rate • Chemotherapy completion rate
Study Design	Multinational, multicenter, retrospective, observational study
Statistics	Patient demographics and treatment parameter will be described using descriptive statistics. Overall survival (OS) will be calculated from the beginning of (chemo)radiotherapy until death, while progression-free survival (PFS) is defined as time interval between start of (chemo)radiotherapy until death, local/locoregional or distant progression. The Kaplan-Meier method will be used to calculate OS and PFS, and groups will be compared using log-rank tests. Both uni- and multivariate Cox proportional hazard regression analyses will be performed to analyze the prognostic role of several patient- und treatment-related parameters including chemotherapy administration on survival. In order to control for potential confounder variables, both matching-pair and propensity score matching approaches are aimed to conduct.
Enrollment	1000 anticipated
Study Completion	June 2022

3. PIs – Funding

PI: Prof. Dr. Dr. Nils H. Nicolay, M.D., Ph.D.

Junior-PI: Dr. Alexander Rühle, M.D.

Funding: No external funding

4. Brief Summary

The number of elderly head-and-neck squamous cell carcinoma (HNSCC) patients is increasing; however, the evidence regarding the ideal treatment for this often vulnerable and frail patient cohort is limited. Although the benefit of concomitant chemotherapy has been reported to decrease in elderly HNSCC patients based on the MACH-NC meta-analysis, it remains unknown whether state-of-the art radiotherapy techniques such as intensity-modulated radiotherapy (IMRT), modern supportive treatments and alternative chemotherapy fractionation (e.g., cisplatin weekly) may have altered this observation. The objective of this retrospective multinational multicenter study is to determine the oncological outcomes of elderly patients (≥65 years) with locally advanced HNSCCs undergoing definitive (chemo-)radiation and to investigate the influence of concomitant chemotherapy on overall survival and progression-free survival after adjusting for potential confounder variables such as age, performance status and comorbidity burden.

5. Aims

Multinational multicenter retrospective analysis to reveal the role of concomitant chemotherapy in elderly patients with locally advanced head-and-neck squamous cell carcinoma (HNSCC) undergoing definitive (chemo)radiotherapy. In particular, subgroup analyses based on age, performance status and comorbidity burden are planned in order to define the benefit of chemotherapy in distinct subgroups. Furthermore, patterns-of-care regarding the administration of concomitant chemotherapy will be analyzed within this international cohort.

Outcome Measures:

Primary Outcome Measure:

- Overall survival (OS)

Secondary Outcome Measures:

- Progression-free survival (PFS)
- Type of concomitant chemotherapy
- Cumulative cisplatin dose
- Radiotherapy completion rate
- Chemotherapy completion rate

6. Study Population and Methods

All elderly (≥65 years) head-and-neck squamous cell carcinoma (HNSCC) patients undergoing definitive (chemo)radiotherapy between 2005 and 2019 at a tertiary cancer center will be included and analyzed in terms of overall survival and the potential benefit of concomitant chemotherapy administration.

Methods

The SENIOR study is an investigator-initiated multinational multicenter retrospective observational study aiming to elucidate the value of concomitant chemotherapy in elderly patients with locally advanced HNSCCs undergoing definitive (chemo)radiotherapy. About 1000 patients that received a definitive (chemo)radiotherapy between 2005 and 2019 at tertiary cancer centers in Germany, Switzerland, Cyprus, and the USA will be included.

Patient and treatment data will be collected retrospectively using patient charts. The following criteria will be collected:

- Start of radiation (DD/MM/YYYY)
- End of radiation (DD/MM/YYYY)
- Age at start of radiation
- Gender
- Site of cancer
- T Stage
- N Stage
- HPV status
- Grading
- Tobacco History

- Pack Year history
- Active Smoking During Radiation
- ECOG
- Age Adjusted Charlson Comorbidiity Index
- Hemoglobin at start
- Leukocytes at start
- CRP at start
- Creatinine at Baseline
- GFR
- Weight at baseline
- Planned Radiotherapy Dose
- Planned Radiotherapy Dose
- Planned number of fractions
- Planned total EGD2
- Applied Radiotherapy dose
- Applied Radiotherapy dose to the primary tumor
- Applied number of fractions
- Applied total radiotherapy
- Radiotherapy completed
- Chemotherapy received
- If chemotherapy, which type
- Cumulative Cisplatin
- Chemotherapy Completed
- Death
- Date of Death
- Locoregional Control
- Date of locoregional progress
- Date of distant metastasis progression
- Date of last contact
- Locoregional control
- Time locoregional control in months
- Progression free survival
- Time of progression free survival in months
- Dead or alive
- Time of survival in months

7. Statistics

Patient demographics and treatment parameter will be described using descriptive statistics. Overall survival (OS) will be calculated from the beginning of (chemo)radiotherapy until death, while progression-free survival (PFS) is defined as time interval between start of (chemo)radiotherapy until death, local/locoregional or distant progression. The Kaplan-Meier method will be used to calculate OS and PFS. Groups will be compared using log-rank tests. Both uni- and multivariate Cox proportional hazard regression analyses will be performed to analyze the prognostic role of several patient- und treatment-related parameters including chemotherapy administration on survival. In

order to control for potential confounder variables, both matching-pair and propensity score matching approaches are aimed to conduct.

8. Data Management and Data Protection

Data collection will be conducted at the respective center. Prior to data transfer to the primary center Freiburg, patient data will be pseudonymized (e.g., FR-001). Patient-related data such as name and date of birth will not be shared with the primary center. The list with the assignment between patient name and pseudonymization-code (e.g., FR-001) will be securely stored at the participating center.

Following the rules of good scientific practice, analyzed data sets will be stored for at least 10 years in institutional databases.

9. Participating Centers

- Department of Radiation Oncology, University Medical Center Freiburg, Freiburg, Germany
- Department of Radiooncology, Charité - Universitätsmedizin Berlin, Berlin, Germany
- Department of Radiotherapy and Oncology, J. W. Goethe University, Frankfurt am Main, Germany
- Department of Radiation Oncology, University of Würzburg, Würzburg, Germany
- Department of Radiation Oncology, University Hospital Schleswig-Holstein, Kiel, Germany
- Department of Radiation Oncology, University Medical Center, Johannes Gutenberg University, Mainz, Germany
- Department of Radiation Oncology, University Hospital LMU Munich, Munich, Germany
- Department of Radiation Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany
- Department of Radiation Oncology, University Hospital Zürich, Zürich, Switzerland
- Department of Radiation Oncology, Case Western Reserve University, Cleveland, USA
- Department of Radiation Oncology, Icahn School of Medicine at Mount Sinai, New York, USA
- Division of Radiation Oncology, The Ohio State University Wexner, Columbus, USA
- Department of Radiation Oncology, German Oncology Center, Limassol, Cyprus

10. Signatures

Nils Nicolay Alexander Rühle